60. (New) The method of claim 40, wherein said liposome membrane forming substance is present in an between about 1 to 5%, by weight, of the preparation.

61. (New) The method of claim 40, wherein said liposome membrane forming substance comprises lecithin.

62. (New) The preparation of claim 17, wherein the PVP Iodine is present as a 0.1 to 2 % solution.

63. (New) The method of claim 40, wherein the PVP Iodine is present as a 0.1 to 2 % solution.

REMARKS

Claims 1, 9-14, 16-18, 22-23, 32-51 and 55-63 are pending. Claims 2, 4-8, 24, 26-31 and 52-54 have been canceled without prejudice. Claims 1, 9-12, 16, 17, 22-23, 32-36, 38, 40-41, 44-47, 51 and 55-57 have been amended. Claims 58-63 have been added. Applicants respectfully submit that no new matter has been added by virtue of these amendments.

I. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

In the Office Action, claims 1-2, 4-14, 16-18, 22-24 and 26-57 were rejected under 35 U.S.C. § 112, first paragraph on the grounds of non-enablement. The Examiner stated that "the specification, while being enabled for liposomes containing povidone iodine, does not reasonably provide enablement for generic 'wound healing agent' and 'antiseptic agent' combined with a particulate carrier or various particles claimed in claim 2...."

In response, independent claims 1, 22 and 23 have been amended to recite "liposomes" as the particulate carrier and "povidone iodine" as the active agent. As the Examiner has indicated that the specification is enabled for liposomes and povidone iodine, it is respectfully requested

that the non-enablement rejection be removed.

II. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH:

In the Office Action, claims 2, 4-6, 8, 10, 14, 16, 24, 26, 37, 46-47 and 56-57 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite on several grounds.

Claims 4 and 27 were rejected on the grounds that "the distinction between 'organic disinfectants' and rest of the components such as alcohols, phenols, etc., . . . is unclear." It is noted that claims 4 and 27 have been canceled without prejudice.

Claims 2 and 24 were rejected on the grounds that the "large" is a relative term. It is noted that claims 2 and 24 have been canceled without prejudice.

Claim 8 was rejected on the grounds that the term improperly recites "at least one." It is noted that claim 8 has been canceled without prejudice.

Claim 14 was rejected on the grounds that the terms "conserving agents" and "consistency-forming agents" are indefinite. In response, claim 14 has been amended without prejudice to delete these terms.

Claims 16 and 39 were rejected on the grounds that the terms "compacted solid medicament reservoir" and "ring-tablet" are indefinite and on the Examiner's inquiry of "[w]hat is the difference between a suspension and a dispersion" and "how can [the preparation] be in solution form." In response, the terms "ring-tablet", "suspension" and "solution" have been deleted without prejudice, and the term "compacted solid medicament reservoir" has been amended to recite "tablet."

Claim 26 was rejected on the grounds that "the claim recites anti-inflammatory agents and then recites the same combination of active agents recited in the parent claim." It is noted that claim 26 has been canceled without prejudice.

Claims 55 and 46 were rejected on the grounds of not further limiting the claims from which they were dependent. In response, the dependencies of these claims have been amended in order for the claims to be properly limiting.

In view of the actions taken, the Examiner is respectfully requested to remove indefiniteness rejections.

III. DOUBLE PATENTING REJECTION:

In the Office Action, claims 22-24, 26-43 and 51-57 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 25-26, 29-47 and 51-53 of copending Application No. 09/701,220. As this rejection is provisional, Applicants will consider the filing of a terminal disclaimer in the event the copending claims issue as a United States Patent.

Claims 1-2, 4-14, 16-18 and 40-50 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 5,863,556.

In response, it is noted that independent claim 1 recites that the preparation is "aerosolized or nebulized." It is respectfully submitted that claims 1-25 of U.S. Patent No. 5,863,556 do not teach or suggest to one skilled in the art to disperse the formulations claimed therein to "aerosolized or nebulized" form as recited in the present claims. Accordingly, the Examiner's obviousness-type double patenting rejection in view of the '556 patent should be removed.

IV. REJECTIONS UNDER 35 U.S.C. § 102(b):

In the Office Action, the Examiner rejected claims 1-2, 9-12, 14-16, 19-26, 32, 34-39, 42-44, 46-47, 51, 53-54 and 56-57 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,049,388 ("the Knight patent"). The Examiner stated that "Knight discloses liposome aerosol formulation for the delivery of drugs to respiratory tract...". The particle sizes are 1-5 microns. The drugs include antibiotics, antiviral agents and steroids...."

Claims 1-2, 9-12, 14-16, 19-26, 32, 34-39, 42-44, 46-47, 51, 53-54 and 56-57 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,049,389 ("the Radhakrishnan patent"). The Examiner stated that Radhakrishnan discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-5 microns. The drugs include antibiotics, antiviral agents and steroids...."

Claims 1-2, 9-12, 14-16, 19-26, 32, 34-39, 42-44, 46-47, 51, 53-54 and 56-57 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,290,540 ("the Prince patent"). The Examiner stated that Prince discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-10 microns. The drug combination include antibiotics, antiviral agents and steroids...."

Claims 1-2, 4, 9, 11-12, 14-16 and 44 were rejected under 35 U.S.C. § 102(b) as being anticipated by Schreier (Journal of Controlled Release, 1993). The Examiner stated that "Schreier discloses liposomal compositions containing antimicrobials such as pentamidine, glutathione and superoxide dismutase."

In response, the Examiner is directed to the independent claims of the present invention which recite "liposomes" as the particulate carrier and "povidone iodine" as the active agent. It is respectfully submitted that neither the Knight patent, the Radhakrishnan patent, the Prince patent nor the Schreier reference teach or suggest preparations comprising liposomes and

povidone iodine or methods of administration thereof and the Examiner is requested to withdraw these rejections.

Claims 1-2, 4-14, 16-18 and 44-50 were rejected under 35 U.S.C. § 102(b) as being anticipated by JP-7-145081 or EP 0 639 373. The Examiner stated that the JP and EP references disclose the same composition as the present claims.

This rejection is respectfully traversed. It is submitted that the JP and EP references do not teach or suggest the formulations disclosed therein in nebulized or aerosolized form as recited in independent claim 1 and the Examiner is requested to withdraw these rejections.

V. REJECTION UNDER 35 U.S.C. § 103(a):

In the Office Action, the Examiner rejected claims 1-2, 4-14, 16-18, 22-24 and 26-57 under 35 U.S.C. § 103(a) as being unpatentable over the Knight or the Radhakrishnan or the Prince patents or the Schreier reference. The Examiner stated that "Knight, Radhakrishnan, Prince and Schreier do not teach the administration of all of the claimed compounds and the treatment of wounds caused by different infections. However, since the purpose of Knight, Radhakrishnan, Prince is to administer compounds to the respiratory tract to treat disease conditions in liposomal form, it would have been obvious to one of ordinary skill in the art to use any antiseptic agent or wound healing agent, with a reasonable expectation of success." Furthermore, the Examiner stated that "it is deemed obvious to one of ordinary skill in the art that the wound healing compositions can be applied during any state wherein the wounds are susceptible to infectious agents, with the expectation of similar anti-septic effect."

In response, the Examiner is again directed to the independent claims of the present invention which are limited to "povidone iodine" as the active agent. It is respectfully submitted that neither the Knight patent, the Radhakrishnan patent, the Prince patent nor the Schreier reference provide the motivation for one skilled in the art to prepare formulations comprising

liposomes and povidone iodine as recited in claim 1 or the methods of administering liposomes and povidone iodine as recited in claims 22 and 23.

Claims 4-6, 17-18 and 40 were rejected under 35 U.S.C. § 103(a) as being unpatentable over JP or EP in combination with Knight or Radhakrishnan or Prince or the Schreier reference. The Examiner stated that "one of ordinary skill in the art would have been motivated to use PVP-iodine taught by JP, and EP as a drug in the liposomal compositions of Knight, Radhakrishnan or Prince or Schreier with the expectation of obtaining similar results since PVP-Iodine is a known anti-septic agent as shown by JP and EP."

It is noted that claims 4-6 have been cancelled, with independent claims 1, 22 and 23 being limited to liposomes and povidone iodine.

With respect to the rejection, it is submitted that the Knight, Radhakrishnan, Prince or Schreier references are directed to inhalable preparations and the JP and EP references are directed to compositions and methods for external use. Accordingly, one skilled in the art would not be motivated to combine these references to arrive at the present invention.

Further, as stated by the Examiner, the Knight, Radhakrishnan, Prince and Schreier references describe the administration of "compounds to the respiratory tract to treat disease conditions in liposomal form." However, these references do not teach or suggest that the formulations described therein can be utilized with antiseptic agents. Accordingly, one skilled in the art would not be motivated "to use any antiseptic agent" in the formulations described therein as suggested by the Examiner.

It is respectfully submitted that the use of povidone iodine and liposomes has not been taught or suggested by the prior art to be aerosolized or nebulized as recited in claim 1 or to be administered to the lower respiratory tract as recited in claims 22 and 23. It is further submitted

that the effectiveness of an agent, e.g., an antiseptic such as povidone iodine, by external administration, does not necessarily provide a reasonable expectation of success that the agent can be administered internally, e.g., by inhalation. Accordingly, the Examiner is requested to remove the rejections under 35 U.S.C. § 103(a).

VI. CONCLUSION

Applicants respectfully submit that the pending claims are in condition for allowance. An early and favorable decision on the merits is earnestly solicited.

A check in the amount of $110.00 is enclosed to cover the fee for a one-month extension of time. If it is determined that any additional fees are due or that any fees have been overpaid, the Commissioner for Patents is hereby authorized to charge said fees or credit any overpayment to Deposit Account No. 50-0552.

Respectfully submitted,

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Marked-up Version of Amended Specification:

On page 4, paragraph 6 (lines 22 and 23) have been amended as follows:

The invention further comprises a method of treating the lower respiratory tract, in humans or animals, as defined in claims [21 and] 22 and 23.

Marked-up Version of Amended Claims:

1. (Three Times Amended) A pharmaceutical preparation for [the] application [of antiseptic agents or agents which promote the healing of wounds] to the lower respiratory tract, comprising aerosolized or nebulized inhalable [particulate carriers] liposomes suitable for administration into the lower respiratory tract combined with [an agent selected from the group consisting of an antiseptic agent, a wound-healing agent or a combination thereof] povidone iodine.

9. (Three Times Amended) The preparation of claim 1, wherein the [carrier particles] liposomes have a size in the range of between 1 and about 50 μm.

10. (Three Times Amended) Amended) The preparation of claim 1, wherein the [carrier particles] liposomes have a size in the range of between 20 and about 30 μm for application to the trachea.

11. (Twice Amended) The preparation of claim 1, wherein the [carrier releases] liposomes release the [agent] povidone iodine over an extended time period.

12. (Twice Amended) The preparation of claim 11, wherein the [carrier releases] liposomes release the [agent] povidone iodine at approximately the same release rate over the release time period.

14. (Twice Amended) The preparation of claim 1, wherein the preparation [contains additives and adjuvants comprising conserving agents, antioxidants and consistency-forming] further comprises a pharmaceutically acceptable additive [additives].

16. (Three Times Amended) The preparation of claim 1, wherein, the aerosolized or nebulized [carrier particles] liposomes are derived from a tablet [compacted solid medicament reservoir, a ring-tablet], a gelatin capsule, a powder, a spray, an emulsion, [a suspension] or [a solution] a dispersion containing the [carrier] liposomes and [agent or agents] povidone iodine in a pharmaceutically acceptable solid or liquid formulation, which is suitable for the generation of inhalable particles.

17. (Three Times Amended) The preparation of claim 1, wherein said [particulate carrier] preparation comprises:

(a) liposomes comprising a pharmaceutically acceptable liposome membrane forming substance; and

(b) between 0.1 to 10%, by weight, [a 0.1 to 2%] PVP iodine [solution], wherein the liposomes are in a size between about 1μm and about 50μm.

22. (Three Times Amended) A method of treating infections of the lower respiratory tract in a human or animal comprising administering a pharmaceutical preparation to the lower respiratory tract, said preparation comprising [an] inhalable [particulate carrier] liposomes combined with [an agent selected from the group consisting of an antiseptic agent, a wound-healing agent or a combination thereof] povidone iodine.

23. (Three times Amended) A method of providing functional tissue remodeling and repair in the lower respiratory tract in a human or animal comprising administering a pharmaceutical preparation to the lower respiratory tract comprising liposomes [an inhalable particulate carrier] combined with povidone iodine [an agent selected from the

group consisting of an antiseptic agent, a wound-healing agent or a combination thereof].

32. (Three Times Amended) The method of claim 22 or 23, wherein the [carrier particles] liposomes have a size in the range between about 1 μm and about 50 μm.

33. (Three Times Amended) The method according to claim 32, wherein the [carrier particles] liposomes have a size in the range between 20 μm and 30 µm diameter for application to the trachea.

34. (Twice Amended) The method of claim 22 [or 23], wherein [that] the [carrier releases] liposomes release the [agent] povidone iodine over an extended time period.

35. (Twice Amended) The method of claim 22 [or 23], wherein the [carrier releases] liposomes release the [agent] povidone iodine at approximately the same release rate over the release time period.

36. (Amended) The method of claim 22 [or 23], wherein the preparation additionally comprises at least one [anaesthetically] anesthetically active agent.

37. (Amended) The method of claim 22 or 23, wherein the preparation [contains additives and adjuvants comprising conserving agents, antioxidants and consistency-forming] further comprises pharmaceutically acceptable additives.

38. (Three Times Amended) The method of claim 22 or 23, wherein the [particulate carrier is] liposomes are suitable for administration via nebulization or [aerolsolization] aerosolization.

39. (Twice Amended) The method of claim 22 or 23, wherein the preparation comprises a tablet [compacted solid medicament reservoir, a ring-tablet], a gelatin capsule, a powder, a spray, an emulsion, or a dispersion [a suspension a solution] containing the [carrier] liposomes and [agent or agents] povidone iodine in a pharmaceutically acceptable solid or liquid formulation, which is suitable for the generation of inhalable particles.

40. (Twice Amended) The method of claim 22 [or 23], wherein said [particulate carrier] preparation comprises:

(a) liposomes comprising a pharmaceutically acceptable liposome membrane forming substance; and

(b) between 0.1 to 10%, by weight [a 0.1 to 2%] PVP iodine [solution], wherein the liposomes are in a size between about 1μm and about 50μm.

41. (Three Times Amended) The method of claim [22 or 23] 40, wherein the liposomes are in a size range between 20 μm and 30 μm diameter for application to the trachea.

44. (Twice Amended) The preparation according to claim 9, wherein the [carrier particles] liposomes have a size in the range between 1μm to about 30μm.

45. (Twice Amended) The preparation according to claim 10, wherein the liposomes [carrier particles] have a size in the range between about 10μm and 20μm diameter for application to the bronchi.

46. (Twice Amended) The preparation according to claim 1 [10], wherein the liposomes [carrier particles] have a size in the range between 1μm and 6μm diameter for application to the alveoli.

47. (Twice Amended) The preparation according to claim 10, wherein the liposomes [carrier particles] have a size in the range between 2μm and 5μm diameter for application to the alveoli.

51. (Amended) The method of claim 22 or 23, wherein the liposomes [carrier particles] have a size in the range between about 1μm and about 30μm.

55. (Twice Amended) The method of claim 22 or 23, wherein the liposomes have a size in the range between 10μm and 20μm diameter for application to the bronchi.

56. (Twice Amended) The method of claim [55] 22, wherein the liposomes have a size in the range between 1μm and 6μm diameter for application to the alveoli.

57. (Twice Amended) The method of claim [56] 22, wherein the liposomes have a size in the range between 2μm and 5μm diameter for application to the alveoli.